DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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February 9, 2015

Silk Road Medical, Inc
Mr. Richard Ruedy
Executive Vice President, RA/CA/QA
735 North Pastoria Ave
Sunnyvale, California 94085

Re: K143072
Trade/Device Name: ENROUTE Transcarotid Neuroprotection System
Regulation Number: 21 CFR 870.1250
Regulation Name: Percutaneous Catheter
Regulatory Class: Class II
Product Code: NTE
Dated: January 5, 2015
Received: January 7, 2015

Dear Mr. Ruedy,

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in

the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Kenneth J. Cavanaugh -S

for

Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

Indications for Use Statement

510(k) Number (if known): K143072

Device Name: ENROUTE Transcarotid Neuroprotection System

Indications for Use:

ENROUTE Transcarotid Neuroprotection System is intended to provide transcarotid vascular access, introduction of diagnostic agents and therapeutic devices, and embolic protection during carotid artery angioplasty and stenting procedures for patients diagnosed with carotid artery stenosis and who have the appropriate anatomy described below:

- Adequate femoral venous access
- Common carotid artery reference diameter of at least 6 mm.
- Carotid bifurcation is a minimum of 5 cm above the clavicle as measured by duplex Doppler ultrasound (DUS) or computerized axial tomography (CT) angiography or magnetic resonance (MR) angiography

Prescription Use __X__ **Or** **Over-The-Counter Use _____**

(per 21 CFR 801.109)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED

Concurrence of CDRH, Office of Device Evaluation (ODE)

510(k) Summary

I. SUBMITTER

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Date Prepared
October 24, 2014

II. DEVICE

Name of the Device: ENROUTE™ Transcarotid Neuroprotection System
Common or Usual Name: Temporary carotid catheter for embolic capture
Classification Name: Percutaneous Catheter (21 CFR§ 870.1250)
Regulatory Class: Class II
Product Code: NTE

III. PREDICATE

W.L. Gore & Associates, Inc. Gore Flow Reversal System (K083300)
This predicate has not been subject to a design-related recall.
No reference devices were used in this submission.

IV. DEVICE DESCRIPTION

Silk Road Medical, Inc. is the manufacturer of a single use device intended to provide embolic protection during carotid artery angioplasty and stenting procedures. The ENROUTE Transcarotid NPS is designed to transport emboli away from the carotid artery circulation by reversing blood flow at the treatment site prior to crossing a lesion in the carotid artery and during lesion manipulation. It has an in-line filter used to capture and contain embolic material liberated during the procedure.

The ENROUTE Transcarotid NPS consist of three primary components: the ENROUTE Transcarotid Arterial Sheath (Model #1016), the ENROUTE Venous Return Sheath (Model #1026), and the ENROUTE Flow Controller (Model #2031). When assembled, the ENROUTE Transcarotid NPS creates an Arteriovenous Shunt. The Transcarotid Arterial Sheath is placed in the carotid artery below the carotid bifurcation. The Venous Return Sheath is placed into the femoral vein. The Arterial and Venous Sheaths are connected by the Flow Controller, thereby completing the Arteriovenous Shunt. When the carotid artery is occluded just proximal to the Transcarotid Arterial Sheath insertion site, the arterial/venous pressure gradient diverts or reverses the internal carotid artery (ICA) and external carotid artery (ECA) blood flow thereby directing the blood from the cerebral arteries through the Transcarotid Arterial Sheath, through the Flow Controller, and out through the through the Venous Return Sheath into the venous circulation. The ENROUTE Transcarotid NPS is an ethylene oxide sterilized, non-pyrogenic, single-use prescription device.

The associated accessory for use with the ENROUTE Transcarotid NPS is an FDA cleared 0.038” guidewire (K890959). The guidewire is used to facilitate the insertion of the Transcarotid Arterial Sheath into the common carotid artery (CCA) and the Venous Return Sheath into the femoral vein.

V. INDICATIONS FOR USE

ENROUTE Transcarotid NPS is intended to provide transcarotid vascular access, introduction of diagnostic agents and therapeutic devices, and embolic protection during carotid artery angioplasty and stenting procedures for patients diagnosed with carotid artery stenosis and who have the appropriate anatomy described below:

- Adequate femoral venous access
- Common carotid artery reference diameter of at least 6 mm.

- Carotid bifurcation is a minimum of 5 cm above the clavicle as measured by duplex Doppler ultrasound (DUS) or computerized axial tomography (CT) angiography or magnetic resonance (MR) angiography

The Indications for Use statement for the ENROUTE Transcarotid NPS device is not identical to the Predicate Device; however, the differences do not alter the intended therapeutic use of the device nor do they affect the safety and effectiveness of the device relative to the predicate. Both the Subject Device and the Predicate Device have the same intended use for embolic protection during carotid artery angioplasty and stenting procedures.

VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

The Subject Device and Predicate Device are both embolic protection systems featuring vascular proximal occlusion and reversal of flow at the treatment site as the means to prevent emboli from reaching distal vasculature during a carotid intervention. The Subject and Predicate Devices are sterile, disposable, single-use devices. At a high level, the Subject and Predicate Devices are based on the following same technological elements:

- Target anatomical site: lesions in the Internal Carotid Artery with or without involvement of the Common Carotid Artery
- Create vascular occlusion
- Use of embolic filter
- Reverse blood flow at the treatment site of the Internal Carotid Artery.

The following technological differences exist between the Subject Device and Predicate Device:

- Access site: Femoral Access for the Predicate Device and Carotid Access for the Subject Device
- Method of closure: Percutaneous closure device or manual compression for the Predicate Device and Suture closure under direct visualization for the Subject Device

The technological characteristics and principals of operation of the ENROUTE Transcarotid NPS is substantially equivalent to the named predicate device.

VII. PERFORMANCE DATA

Performance Testing was performed in accordance to Guidance for Industry and Food and Drug Administration Staff *Coronary and Carotid Embolic Protection Devices Premarket Notification [510(k)] Submissions* dated February 15, 2008 The following performance testing was conducted on the ENROUTE Transcarotid NPS to support a determination of substantial equivalence to the predicate device.

Biocompatibility

The biocompatibility evaluation for the ENROUTE Transcarotid NPS was conducted in accordance with the FDA Blue Book Memorandum #G-95-1 "Use of International Standard ISO 10993, Biological Evaluation of Medical Devices Part 1: Evaluation and Testing,'" May 1, 1995, and International Standard ISO 10993-1 "Biological Evaluation of Medical Devices- Part 1: Evaluation and Testing Within a Risk Management Process," as recognized by FDA. The battery of tests included the following tests:

- Cytotoxicity: MEM Elution L-929 ISO/USP
- Sensitization: Murine LLNA
- Irritation: ISO Intracutaneous Reactivity Test
- Systemic Toxicity: ISO Acute Systemic Injection
- Hemocompatibility:
    - Four Hour Thromboresistance Evaluation in Dogs
    - Complement Activation C3a and SC5b-9
    - Platelet and Leukocyte Count
    - Partial Thromboplastin Time
    - Hemolysis
- Genotoxicity:
    - Bacterial Mutagenicity Test- Ames Assay
    - *in vitro* Mouse Lymphoma Assay
    - *in vivo* Mouse Micronucleus Assay
- Pyrogenicity
    - Material Mediated Pyrogen
    - Bacterial Endotoxins-Limulus Amebocyte Lysate (LAL)

The ENROUTE Transcarotid NPS is considered to be a circulating blood external communicating device with limited exposure (≤ 24hr). Exceptions include the non-patient contacting components which are assembled around the outside of the blood-path tubing and include the Flow Controller (with filter) components, low flow line coil clip, and heat shrink tubing.

Bench Testing

- Visual Inspection and Dimensional Verification
- Disengagement Force Dilator to Hemostasis valve
- Force to Advance and Retract Guidewire through Dilator

- Dilator Hub Functional Testing (ISO 594-1)
- Sheath Stopper Removal
- Kink Resistance
- Hemostat Clamp and Unclamp
- Air Leakage During Aspiration (ISO 10555-1)
- Liquid Leakage Under Pressure (ISO 10555-1 and ISO 11070)
- Hi/Lo Switch Cycling
- Flow Stop Button Cycling
- Guide Wire Integrity (ISO 10555-1 and ISO 11070)
- Tensile Tests
- Flow Rate Characterization
- Flow Patter Characterization
- Air Emboli and Solid Emboli Transportation Simulation
- Small and Large Particle Transport and Capture Efficiency
- System Preparation and Simulated Use
- Packaging Validation (ISO 11607-1 and ISO 11607-2)
- Sterilization Validation (ISO 11135-1:2007)
- Shelf Life

Animal Studies

A series of GLP animal studies were performed to evaluate the safety, performance and handling of the ENROUTE Transcarotid Neuroprotection System as compared to a control device (Gore Flow Reversal System (K083300)) in both ovine and porcine models. Based on pathology and histopathology results, the safety acceptance criteria for the studies were met. Performance and handling observations were made based on detailed characteristics of the device. No untoward observations were found by the clinician.

Clinical Performance Testing

The ROADSTER study is a prospective, single-arm, multi-center clinical trial of the ENROUTE Transcarotid Neuroprotection System in conjunction with all commercially approved carotid artery stents used for revascularization in patients with carotid disease who are at high risk for complications from carotid endarterectomy (CEA). There was a lead-in phase of up to five (5) patients per Investigator to allow Investigators to gain experience with the study device prior to pivotal study enrollment. Seventeen (17) sites in the United States of America and one (1) in the European Union participated in the study under IDE G120143.

Sixty-seven (67) lead-in and one hundred forty-one (141) pivotal subjects at high risk for complications from CEA were enrolled between November 2012 and July 2014.
The intent of this study was to establish the safety and effectiveness of the Subject Device in providing cerebral embolic protection during angioplasty and stenting procedures in carotid arteries in subjects at high risk for complications from CEA.

The Subject Device also facilitates access to the carotid and neuro anatomy for the introduction of therapeutic or diagnostic endovascular devices and/or agents.

Subjects were followed for 30-days post procedure. Subjects who were suspected of having a stroke were asked to return at 3 months post procedure for a follow-up neurological exam. Subjects suspected of having a procedure related cranial nerve injury were asked to return at 6 months post-procedure for a follow up neurological examination.

Primary Endpoint: The primary endpoint is a hierarchical composite of any stroke, myocardial infarction and death during a 30-day post-procedural period in the ITT (pivotal) population comprised of subjects deemed to be at high risk for complications from CEA.

Secondary Endpoints: The following secondary endpoints will be assessed 0 to 30 days in the ITT (pivotal) population comprised of subjects deemed to be at high risk for complications from CEA:

- Technical success
- Acute Device success
- Procedural success
- Access Site Complications
- All death
- All stroke
- All MI
- Cardiac death
- Ipsilateral stroke
- Contrast Usage

Effectiveness:

The study population enrolled in the ROADSTER study was comparable to other contemporaneous studies of CAS and embolic protection devices (EPDs). In addition to inclusion of subjects deemed to be at high risk for complications from CEA, the demographics and baseline characteristics, medical history, cardiopulmonary history, neurological history reflect similar populations. The study met its primary endpoint because the upper 95% confidence interval of the observed primary endpoint event rate (3.5%) was significantly lower that the performance goal of 11% (p=0.0047).

Technical success, acute device success, procedural success and procedural access site complications were calculated and presented using counts, percentages,

and exact 95% binomial confidence intervals. Acute device success was 99.3% (140/141, 95% CI 96.57%, 99.88%). Technical success was 99.3% (140/141, 95% CI 95.84%, 99.70%).

Safety:

For the Subject Device, 14.2% of patients had one or more serious adverse events. Adverse events for both the Subject Device and the Predicate Device included access site complications (hematoma, vessel dissection, hemorrhage), hypotension and stent thrombosis. In all adverse events, 9.5% of the events were unrelated to the device, 1.2% possibly related to the device, 2.4% probably related to the device and 3.7% related to the device.

Summary:

Based on the clinical performance as documented in the pivotal clinical study, the ENROUTE Transcarotid NPS was found to have a safety and effectiveness profile that is similar to the Predicate Device.

VIII. CONCLUSIONS

Since the Predicate Device was cleared based in part on the results of clinical studies, and since comparison of bench testing to clinical outcomes is still not well understood for this type of device, clinical testing was required to support substantial equivalence. The non-clinical data support the safety of the device and the verification and validation demonstrate that ENROUTE Transcarotid NPS should perform as intended in the specified use conditions. The clinical data demonstrate that the ENROUTE Transcarotid NPS performs comparably to the Predicate Device that is currently marketed for the same intended use.